

REMARKS

Upon entry of the present amendments, claims 7-12, 15, 19-28, 32-39 and 43-48 are pending in this application. Claims 7, 9, 12, 26 and 27 have been amended for formal reasons as shown above. It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested. By the amendments, Applicant does not acquiesce to the propriety of any of the Examiner's rejections and does not disclaim any subject matter to which Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997). Further, Applicant reserves the right to prosecute the subject matter of any canceled claim in one or more continuation, continuation-in-part, or divisional applications.

The Rejection under 35 U.S.C. § 112 Should be Withdrawn

Rejections previously made by the Examiner were withdrawn. However, claims 15, 19, 20, 26-39 and 45-48 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking description for the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease." Applicant respectfully traverses this rejection. The attention of the Examiner is respectfully directed to, for example, page 2, lines 19-26 of the specification:

Persistent, unregulated angiogenesis occurs in a multiplicity of disease states, tumor metastasis and abnormal growth by endothelial cells and supports the pathological damage seen in these conditions. ***The diverse pathological states created due to unregulated angiogenesis have been grouped together as angiogenic dependent or angiogenic associated diseases.*** Therapies directed at control of the angiogenic processes could lead to the abrogation or mitigation of these diseases. (emphasis added)

In addition, the attention of the Examiner is respectfully directed to, for example, page 8, lines 30-32, which relate in part that "it is an object of the present invention to provide a compound and method ***to inhibit ... angiogenesis*** in a human or animal" (emphasis added). These sections of the specification, among others, provide adequate written description support for the phrases "inhibiting angiogenesis" and "treating angiogenesis dependent disease."

Claims 9 and 12 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly failing to define the invention in the required manner. This rejection should be withdrawn in view of the amendments to claims 9 and 12 made herein.

Claims 7, 26 and 27 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. This rejection should be withdrawn in view of the amendments to claims 7, 26 and 27 made herein.

The Rejection of Claims 7-12, 15, 19-39 and 43-48 under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 7-12, 15, 19-39 and 43-48 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over WO 95/03807 ("Billson"). Paper No. 27 at pages 4-6. Applicant respectfully traverses the rejection for the reasons discussed below.

Claims 7-12, 15, 19-39 and 43-48 relate to, *inter alia*, compositions and/or methods of treatment of angiogenesis and angiogenesis related diseases using an angiogenesis inhibiting compound and an anti-inflammatory compound.

As an initial matter, Billson does not teach or suggest the inventions recited by the present claims. While Billson may allegedly relate certain methods of treating inflammatory responses in the macula of the eye, it utterly fails to teach or suggest methods encompassed by the pending claims. Indeed, Billson does not teach or suggest using the compounds encompassed by the pending claims for any purpose whatsoever.

Furthermore, the Examiner has not provided support, based on the references of record, for the contention that one of ordinary skill in the art "is provided with the motivation to utilize any agent that is an angiogenesis agent [sic], which would obviously embrace thalidomide as well as its derivatives and analogues." Paper No. 27 at page 5. For example, the Examiner has not provided the support, based on the references of record, for the contention that it would be "obvious to the skilled artisan to treat ... various ... conditions with angiogenesis inhibitors." Paper No. 27 at page 5. To support this contention, the Examiner appears to have improperly cited the present application, rather than the references of record. Paper No. 27 at page 5. Indeed, the Examiner's appears to be using a type of hindsight reconstruction long proscribed by the United States Court of Appeals for the Federal Circuit.

The Examiner has also not provided the requisite support, based in the references of record, for his apparent contention that the skilled artisan would have been motivated to utilize agents other than thalidomide (*e.g.*, its derivatives and analogues) in pharmaceutical compositions, as long as the agents maintain the pharmaceutical properties of anti-inflammatory agents as well as anti-angiogenesis agents. Paper No. 27 at page 6. Indeed, the Examiner appears to improperly suggest that it would have been obvious for one

of ordinary skill in the art to try any number of compounds in a given therapeutic method or in a given therapeutic composition. For this reason alone, the pending rejections under 35 U.S.C. § 103 must be withdrawn, as it is well settled that whether or not something may have been "obvious to try" cannot form the basis for a proper obviousness rejection. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986) (citing *Jones v. Hardy*, 727 F.2d 1524, 1530 (Fed. Cir. 1984) ("obvious to try" is improper consideration in adjudicating obviousness issue)).

Applicant respectfully assert that mere knowledge that certain compounds may allegedly decrease inflammation and/or angiogenesis would not lead one of ordinary skill in the art to Applicant's discoveries, which were disclosed and claimed for the first time in the present application. Accordingly, Applicant respectfully requests that the rejection of claims 7-12, 15, 19-39 and 43-48 under 35 U.S.C. § 103(a) be withdrawn.

The Rejection of Claim 9 under 35 U.S.C. § 103(a) Should be Withdrawn

Claim 9 stands rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Billson in combination with United States Patent No. 5,348,942 to Little II *et al.* ("Little"). Paper No. 27 at pages 5-8. Applicant respectfully traverses the rejection for the reasons discussed below.

Claim 9 relates to, *inter alia*, compositions using an angiogenesis inhibiting compound and an anti-inflammatory compound.

As an initial matter, and as noted above, Billson neither teaches nor suggests the compounds encompassed by the pending claims. Little fails to rectify this fatal error. Indeed, the Examiner has not established that Little even mentions thalidomide, let alone the particular compounds to which the pending claims are drawn. For this reason alone, the pending rejection under 35 U.S.C. § 103 should be withdrawn.

In addition, the Examiner appears to broadly allege that one of ordinary skill in the art would be motivated by the alleged teachings of Billson in combination with the alleged teachings of Little to utilize an anti-inflammatory agent along with an anti-angiogenesis agent and/or to produce a composition comprising Applicant's specific compounds with an anti-inflammatory agent. Paper No. 27 at pages 6-8. However, as noted above, the Examiner has not provided the requisite support, based in the references of record, for his apparent contention that the skilled artisan would have been motivated to use compounds other than thalidomide—not to mention the particular compounds to which the

pending claims are directed—in a pharmaceutical composition, much less in the methods encompassed by the pending claims.

Furthermore, Applicant respectfully submits that the Examiner has not demonstrated why or how one of ordinary skill in the art would have been motivated to combine Billson with Little, much less to arrive at the presently claimed inventions. The Examiner has provided no reference that makes any connection whatsoever between the alleged teachings of Billson and the alleged teachings of Little. Similarly, the Examiner has not met his burden of demonstrating how the combination of Billson and Little would have provided one of ordinary skill in the art with a reasonable expectation of successfully obtaining the claimed invention.

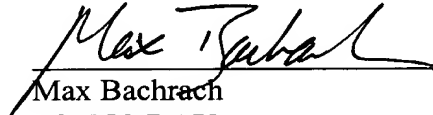
The Examiner appears to contend that when the angiogenesis inhibitory composition is represented by the Applicant's compounds P, Q, R or S in claim 9, that one of skill in the art would recognize that these compounds would easily produce thalidomide via an internal cyclization reaction. The Examiner has provided to Applicant no reference to support this contention. Yet, section 2144.03 of the Manual of Patent Examining Procedure (M.P.E.P.) requires that if the Examiner is relying on personal knowledge to support the finding of what is allegedly known in the art, the Examiner must provide an affidavit or declaration or reference setting forth specific factual statements and explanation to support the finding. As the Examiner has not provided a single reference or an affidavit to support his contention that compounds P, Q, R or S would readily cyclize to thalidomide, Applicant respectfully invites Examiner to provide such a reference or file an Affidavit pursuant to 37 C.F.R. § 1.104(d)(2). In the absence of such a reference or affidavit which is, of course, subject to rebuttal by Applicant, these contentions do not support the rejection over Billson in combination with Little.

Even if one were to assume, for the sake of argument, that those of ordinary skill in the art would have understand how to produce thalidomide via internal cyclization of compounds P, Q, R, or S—a point that Applicant does not concede—the production of thalidomide is irrelevant to the present claims. As the Examiner correctly notes (Paper No. 27 at page 8), the pending claims *exclude* thalidomide. Accordingly, Applicant respectfully requests that the rejection of claim 9 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicant respectfully requests that the above remarks and accompanying documents be entered in the present application file. An early allowance of the present application is respectfully requested.

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